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CENTER FOR BIOLOGICAL SEQUENCE ANALYSIS

The Center for Biological Sequence Analysis (CBS) at the Technical University of Denmark (DTU), Department of Systems Biology, conducts basic research in the general fields of bioinformatics and systems biology. CBS represents one of the largest, multi-disciplinary basic research groups within bioinformatics and systems biology in academia in Europe. Research at CBS is conducted in 11 specialist research groups spanning the broad spectrum of research at the interface between computational biology and wet lab experimentation. CBS is highly active across the spectrum from molecular level disease systems biology, chemical biology, regulatory genomics, evolutionary analysis, and immunological bioinformatics to protein post-translational modifications and sorting. Activities span all kingdoms of life and also their interaction and co-existence, for example in projects on the bacterial flora in the human gut as it is studied using metagenomics and metatranscriptomics techniques. The center is also interfacing to the general area of medical informatics analyzing data from the healthcare sector, including text mining of electronic patient records and biobank questionnaires.

EXPLOITING DATA

Comprehensive public databases of DNA and protein sequences, genotyping, macromolecular structure, gene and protein expression levels, protein-protein interactions, pathway organization and cell signaling, have been established to optimize scientific exploitation of the explosion of data within biology. Among contemporary bioinformatics concerns are reliable computational interpretation of a wide range of experimental data, and the detailed understanding of the molecular apparatus behind cellular mechanisms of sequence information - not only in general terms but also at the level of human individuals. By exploiting available experimental data and evidence in the design of algorithms, sequence correlations and other features of biological significance can be inferred.

WEB SERVICES

A key activity at the Center for Biological Sequence Analysis is the maintenance and further expansion of our web services comprising a large number of computational methods and databases. These are made freely available for academic use and are also available on a commercial basis for industrial use. All the services are available for direct online use, and most are also available as software packages for download and as SOAP based web services.

PARTNERSHIPS

CBS has strong partnerships both nationally and internationally. CBS is a part of the Department of Systems Biology at DTU, which represents the largest concentration of biotech research in Denmark. CBS works closely with the Novo Nordisk Foundation Center for Protein Research at the University of Copenhagen, and also with the Novo Nordisk Foundation Center for Biosustainability at DTU. The close relationship between the centers offers a wide range of opportunities for collaboration on projects and for exchange of staff.

CORE FACILITY

CBS maintains an experimental DTU core facility for the high-throughput analysis of genomic-level events. The core facility is hosted by CBS, however, the core is a DTU wide facility contributing to the research of many other centers and departments at DTU as well as external customers from academia and industry across the country and abroad.

FUNDING AND HISTORY

Based on bioinformatics efforts started in the late 1980s, the group was established formally as a center in 1993 by a large five-year grant from the Danish National Research Foundation. The original grant was extended for an additional five-year period, and since 2003 the Center for Biological Sequence Analysis has relied on an increasing number of grants from different sources as well as a substantial, permanent contribution from the Technical University of Denmark. Major funding agencies and foundations include (but are not limited to): The Danish Research Councils, EU, NIH, the Danish Center for Scientific Computing, the Villum Foundation, the Novo Nordisk Foundation and the Lundbeck Foundation.
The Cancer Systems Biology group is developing computational methods to analyze genome scale molecular profiles of cancer samples in order to improve therapeutic efficacy and find new therapeutic targets. We aim to understand certain key aspects of cancer biology by combining data from a wide variety of sources such as gene expression microarrays, CGH arrays, high-throughput sequencing etc.

Genome scale analysis of cancer helps researchers to expand their research focus from a few genes to a more complete view of the entire cancerous genetic network. The expression levels or DNA copy number of virtually all genes in a cell can be quantified simultaneously. This more complete analysis of human cancer cells will very likely hold the key to solving the difficulties associated with the fact that cancer cells comprise complex, robust and evolving systems.

The group is focusing on several aspects of genome scale analysis of human cancer. Firstly, the group is developing bioinformatics methods that increase the accuracy of high-throughput measurements. Secondly, from the data sets of increased accuracy the aim is to extract quantitative measures of key biological processes in cancer. We are particularly interested in the various subtypes of genomic instability, their relative level in a given tumor and whether this could guide more effective therapeutic decisions. Thirdly, we are combining genome scale molecular profiling of chemotherapy resistant breast cancer cell lines with bioinformatics analysis in order to determine whether clinical response to chemotherapy in cancer can be predicted by gene expression signatures derived from cell lines. The most immediate outcome of this research is to develop tools that would predict with high accuracy which cancer patient will respond to a given chemotherapeutic agent.
**CELLULAR SIGNAL INTEGRATION**

**GROUP LEADER: DR. RUNE LINDING, LINDING@CBS.DTU.DK**

The Cellular Signal Integration Group conducts computational and quantitative biology with the aim of understanding biological signaling systems. We explore biological systems by developing and deploying computational algorithms aimed to predict cell behavior similar to weather forecasts or aircraft models. Cellular signaling networks are the foundation of cell fate and behavior and their aberrant activity is a key mechanism underlying the pathological behavior of cells, such as during tumor development. However, signaling networks are highly complex, involving a vast ensemble of dynamic interactions that flux in space and time.

To understand how normal signal integration and aberrant cell decisions arise requires a global view of cell signaling networks. We and others have demonstrated that predictive insight into a biological system can be obtained through a combination of experimental and computational exploration. Thus, a major aim of our group is to develop computational tools (such as our flagship algorithms NetworKIn) and to deploy these on quantitative mass-spectrometry, genetic and phenotypic data to understand at a systems level principles underlying the spatiotemporal assembly of mammalian signaling networks and how they process information (molecular logic) in order to alter cell behavior (cellular logic). We have previously deployed these algorithms on quantitative proteomics data to model JNK regulation DNA damage response, stem-cell differentiation, cell-cell communication, signaling evolution and to compare model organisms.

A major current activity is the search for signaling networks that drive regulatory diseases such as cancer, diabetes, and neurological disorders. We hypothesize that these networks are powerful therapeutic targets, and we are motivated by the opportunity to perform systems level targeting of complex human diseases while at the same time gaining insights into the fundamental principles behind cellular information processing and decision making.
Several thousand bacterial genome sequences are available in the public databases and more genomes are being sequenced on a daily basis. The Comparative Microbial Genomics (CMG) group explores relationships between large numbers of sequenced bacterial genomes, with emphasis on minimal genomes and genome-based classification methods.

The approach is “genome-centric” in that the DNA sequence is used as the starting material, for example to predict DNA structures, which can in turn be indicators of useful biology, such as localization of a promoter based on DNA curvature and melting profiles, and the prediction of potential genomic island regions. Further, we are developing pipelines to go from genomic sequences to predicted RNAs and proteins in a standardized and consistent manner across all families of bacteria. Soon it will be routine to sequence a hundred or more bacterial genomes a week. This will generate very large amounts of data and that is something we keep in mind when developing pipelines.

The two major focus areas of the group are: 1) minimal genomes – that is, what set of gene families are common to all life; 2) using genomic sequences (and the core/pan-genomes) to predict taxonomic relationships, both at the broad level, such as phyla, or genus/species and also for strain typing and classification.

Handling and maintaining this large amount of data for thousands of organisms sequenced requires a structured database system. For this purpose, the GenomeAtlas database was developed in 1999 and has been updated on a regular basis since then. A recent addition to the atlas pages is the zoomable atlases.

The CMG group has published more than 100 papers since 2000, and the popular DTU course on Comparative Microbial Genomics has been running for more than 10 years, and one-week workshops based on this course are held in North and South America, Europe, Asia, and Africa.
Common human diseases result from the interplay of many genes and environmental factors. A drug – or a xenobiotic agent in general – rarely acts on one target alone but rather follows a complex interaction pattern with a number of proteins. This multi-targeting can be beneficial in drug discovery (polypharmacology), but it may also lead to disturbance of the metabolism, adverse effects or toxic effects. Designing safe and effective medicines requires an in-depth understanding of their phenotypic effect on the human body. Although many questions still remain, systems biology has already led to great advances in our understanding of the biology of complex diseases and drug targets. Thus, the field has now reached a state that allows the integration of large-scale data across multiple levels of information to decipher the effect of small molecules on biological systems. Such efforts are gradually emerging under the name of “systems chemical biology”, with the aim to unravel the genetic background of diseases and to provide the best possible medicinal treatment.

The Computational Chemical Biology (CCB) group has evolved from the former group of Chemoinformatics, with interest in exploring the interplay between small molecules and biological systems using computational methods. The group holds expertise in molecular modeling, machine learning methods (QSAR, Neural Networks, Support Vector Machines), chemogenomics, and systems chemical biology. The overall aim of the research focus of CCB is to elucidate the biological profile of small molecules regarding their targets, off-targets, phenotypic outcome, and side effects through an in-depth understanding of the biological networks that lead to disease. Research topics in the group lie in the areas of drug targets for CNS and metabolic diseases, natural compounds with medicinal properties, ADME-Tox and pharmacogenomics, biological networks for systems pharmacology and clinical effects.

The data warehouse of CCB includes around 600,000 bioactive drugs and drug-like molecules with biologically related annotations and more than 20 million small molecules with structural information. The group also provides online services for the prediction of pH-dependent aqueous solubility of drug-like small molecules, pHSol, and ChemProt, an online resource of annotated and predicted chemical-protein interactions.
Advances in genomic sequencing, both in speed and lower cost, have finally created an opportunity to understand the human genome at the individual level and not just as a composite reference. Variation between individuals can be at the single nucleotide level, stretches of nucleotides or in copy number of sections of the genome. Current estimates indicate that an individual differs by three million single nucleotide polymorphisms (SNPs) from the commonly accepted human reference. Additional sources of variation are alternative splicing of exons within a gene, post-translational modifications (PTMs) on proteins and last but certainly not least, the microbiota within the human being that contributes an important diet-related role.

The mission of the Functional Human Variation group is to understand how this variation translates into function. What individual SNPs influence susceptibility to disease and sensitivity to drug response? Why do some children with leukemia respond well to chemotherapy, but others develop toxic side effects or relapse a few years later? Which mutations in a cancer are drivers and which are passengers? Which nucleotide changes influence protein structural changes or changes in PTMs?

The group works closely with CBS’s Metagenomics group and collaborates with external clinical groups on diseases such as leukemia, breast cancer, male infertility, and childhood asthma. Genotype-phenotype database infrastructure development has been used for these clinical phenotypes as well as non-clinical phenotypes on collaborations with ancient DNA studies. In partnership with DTU’s Multi-Assay Core Facility, the group has developed multiplexed targeted sequencing strategies for low-cost and high-throughput custom genotyping. The group also provides several online machine learning-based prediction methods for signal peptides, protein structural features, and post-translational modifications.
The immune system normally does a good job keeping us free from diseases, but sometimes it fails. One approach towards understanding why this happens is to produce advanced simulation models of the immune system and to understand the relationship between hosts and pathogens in this manner. Depending on the complexity of these models and the input given they can be used to simulate what happens when a host gets infected by a pathogen, thereby predicting the co-evolvement of pathogens and immune systems. One aim of the modeling is to identify the parts of proteins known as epitopes, which are recognized by the immune system, thereby inducing a protective response. This knowledge is very valuable for the development of better vaccines and provides important insights into the nature of cancer, allergy, and autoimmune diseases.

The Immunological Bioinformatics Group is developing new technologies for epitope discovery that can aid in the search for new vaccines and therapies for HIV, malaria, and tuberculosis, as well as for diseases such as influenza and pox, which may evolve to be a threat naturally or intentionally through bioterrorism. The group has built a simulation model of the human immune system and has constructed a database with all human pathogens. Using this database and a database of the human genome, the group is working on using the prediction methods to simulate the co-evolvement of pathogens and immune systems and in particular to identify epitopes from the different arms of immune systems. In most of the projects the predicted epitopes are being validated through experimental collaborations with partners doing wet lab research.

The group has developed methods for the three main types of epitopes: B cell epitopes which are used to recognize microorganisms outside cells; Helper T lymphocyte epitopes which are used to activate cells that have taken up foreign substances; and cytotoxic T lymphocyte epitopes, which are used to detect and kill infected cells.
The study of life at the cellular and molecular level has brought about insight and change beyond anyone’s imagination over the last thirty years. Until quite recently, this type of research has been carried out in a reductionist way in which a few components were studied at a time. However, the latest breakthroughs and advances in nano- and biotechnology have created new possibilities for cataloging and linking hundreds and thousands of biomolecules simultaneously and have thereby paved the way for a new systems-scale view of living cells and organisms. The new field is called systems biology.

The Integrative Systems Biology Group is at the leading edge of these developments, focusing mainly on understanding how intracellular networks of genes, proteins, metabolites and other small molecules regulate cellular behavior and how perturbations to these regulatory systems may lead to disease for the individual.

Our research strategies typically rely on integration of massive amounts of experimental data rather than just on theoretical modeling. Pathways and protein complexes are key levels of analysis helping to understand how genetic changes in many different molecular components lead to the same or similar phenotypes. The ongoing effort in the group is to construct such models that will aid the identification of new disease genes and in uncovering the mechanisms behind complex, multifactorial diseases.

The group also works on combining molecular level systems biology data with medical informatics data from the healthcare sector, such as for example electronic patient records and biobank questionnaires. The aim is to combine and stratify patients not only from their genotypes, but also phenotypically based on the clinical descriptions in the medical records which describe disease histories in detail.
Less than one percent of the known microorganisms can be grown and studied in the lab. With the advent of low-cost high-throughput DNA sequencing technologies it is possible to explore the genetic material from entire microbial communities directly without the need of culturing the organisms under study. This emerging field, known as metagenomics, utilizes a huge genetic reservoir of non-culturable organisms as a resource for biotechnological and medical products and processes. The Metagenomics group collects different samples from all over the world and develops new tools that will address many of the unique challenges of metagenomics data sets.

The majority of our projects are based on at least one of the following three simple questions: Who is in there? What are they doing? How are they doing it?

Our major focus is on metatranscriptomics of the human microbiome – correlating changes in the human microbiome with changes in human health – where we are involved in the EU FP7 project MetaHIT on the metagenomics of the human intestinal tract. We are working in close collaboration with the Molecular and Cellular Evolution of Microbial Eukaryotes group in Newcastle, studying the impact of lateral gene transfer on prokaryotic genome evolution and eukaryotic parasites.

To facilitate the modeling of metabolic and signaling pathways in both prokaryotic and eukaryotic organisms, we are developing new protein features based pipelines based on different machine learning methods. Together with the Functional Human Variation group at CBS, we try to understand the correlation between present day human genetic makeup and human associated bacteria by literally going back in time and studying ancient genomes. This work is carried out in collaboration with the GeoGenetic Center in Copenhagen. The sequencing of complete nuclear genomes of ancient human remains (mummies, skulls, hair tufts from permafrost) and environmental metagenomes from different evolutionary time periods lets us identify the most important milestones during human evolution with respect to changes in the human-microbe interplay. Eventually this may give us insight into present day increased risk of metabolic disorders and other digestive system related diseases.

METAGENOMICS

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Molecular Evolution

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Evolutionary theory is the conceptual foundation of the life sciences. The famous geneticist Theodosius Dobzhansky expressed this very well when he said, “Nothing in biology makes sense, except in the light of evolution”. In the post-genomic era this insight is more relevant than ever, and only by taking the theory of evolution into account is it possible to get a handle on organizing and analyzing the massive amount of biological data now available. In the Molecular Evolution Group we are interested in applying phylogenetic methods to analyze specific biological systems, but also in using the flood of sequence data to learn about the evolutionary process itself.

A focus of much of the research done in the Molecular Evolution Group is the evolution of pathogenic organisms such as HIV, influenza, and the malaria parasite Plasmodium falciparum. In particular, we are interested in how knowledge of the evolutionary processes that occur during infection and transmission of a pathogen can be used as the basis for deriving strategies for fighting the disease. As an example, patterns of sequence variation across a population of influenza viruses close to the time when the virus has jumped from, say, an avian to a human host, will contain information about the selective pressures acting at that point. This knowledge can be directly useful for monitoring when new species jumps are imminent but may also form the basis for designing interventions aimed at hindering such jumps. Our work on pathogen evolution is done in close collaboration with experimental groups at a number of universities and hospitals.

Other projects in the Molecular Evolution Group include investigations into the evolution of resistance to antibiotics, evolution and origin of introns, de novo evolution of genes, and evolution of evolvability (the ability of biological systems to evolve). Generally, we are interested in all aspects of evolution, and while we are very interested in developing and applying state-of-the-art computational tools in our work (especially in the framework of probabilistic model selection and multimodel inference), the focus is always on analyzing problems that are interesting from a biological point of view.
Much of the relationship between genotype and phenotype is determined by gene regulation. The components of signaling and transcriptional regulatory pathways act together in gene regulatory networks (GRNs) to control which genes are expressed, at which times and under which conditions. GRNs are very adaptable within a given individual cell or organism and evolve rapidly to provide large phenotypic diversity over short evolutionary time periods. These networks play critical roles in response to environmental stress, control of normal cell division and proliferation, and when not functioning properly, they contribute to disease progression.

Efforts to understand the regulatory networks in control of stress responses are of particular interest to the Regulatory Genomics Group. In particular, the responses to oxidative and DNA damage stress are being investigated. Although both of these stresses are present at low levels in healthy cells, a measured and rapid stress response must be mounted to ensure survival to acute exposure to these stresses. By perturbing specific regulatory genes, e.g. gene knock-outs or knock-downs, we can observe differences in the regulation of the response using genome-wide mRNA or protein profiles using DNA microarrays, RNA-Seq or mass spectrometry based proteomics analyses. The combination of environmental and genetic perturbations allows us to interrogate GRNs that control these vital cellular responses and provides powerful evidence for the functional role of known and novel regulatory genes.
The Systems Biology of Immune Regulation group studies the role of a deregulation of the innate immune response in initiation of life-style related diseases. Redundant local inflammation due to inappropriate activation of the innate immune system plays a pivotal role in the development of many diseases of affluence, such as coronary heart disease, type 2 diabetes and atopic asthma. The unwanted inflammatory response is also manifested as a low-grade systemic inflammation. In the healthy state, tissue homeostasis is ensured by a tightly controlled balance between pro and anti-inflammatory phenotypes in the tissue-resident immune-cells, which is lost in the initiation of these diseases.

We study how the development of inflammatory responses in specific tissues (e.g. adipose and lung) is dependent on the changes in the functional response pattern of the tissue-resident leukocytes and its modulation by dietary components and the mucosal microbiome. Our specific expertise is how dietary fatty acids and fibers interact in determining the functional immunological response in the tissue through its effects on immune and tissue cell phenotypes as well as the composition of the mucosal microbiome.

We have developed a unique multiplex approach for functional characterization of different immune cell phenotypes on a single cell basis using flow cytometry, which we combine with different omics technologies as well as traditional cell biological and biochemical methods. We apply these methods to integrated studies of primary immune and tissue cell cultures, disease animal models and translational cohort studies in humans aiming at developing systems biology models describing the sequence of events leading to dysregulation of tissue-specific innate immune responses for use in the development of new therapeutic strategies.
Research projects that use a systems biology approach require comprehensive high-throughput analyses that characterize many or all of the components of the system being studied. The set of tools and techniques for analysing DNA and RNA is in constant evolution, involving various trade-offs between high-volume of data, precision and cost. qPCR, microarrays and next-generation sequencing supplemented by flow cytometry are important tools for elucidating biological questions at the systems level offered by DMAC.

The core facility for high-throughput analysis of genomic-level events was established in 2008 at DTU with a substantial grant from the Danish Research Councils and DTU. The core facility is hosted by the Center for Biological Sequence Analysis, but is a DTU wide facility contributing to the research of many other centers and departments at DTU as well as external customers from academia and industry.

The facility provides access to the whole chain that generates knowledge and insight on biological data from genomic or cellular level measurements. Data generation and analysis are technologies, and the core facility is a one-stop shop for getting state-of-the-art work done. Thanks to its unique experience on a range of assays, the DMAC facility can provide advice on the optimal assays, experimental design and subsequent data analysis for each individual project. The aim is to provide the customers with the best in technology and data analysis schemes, while abstracting as many of the technical details as possible.
ABOUT CBS

PUBLICATION PROFILE
CBS has a strong publication profile with more than 750 peer-reviewed papers, many in high impact journals as well as many with very high citation levels. The publication list includes more than a dozen Science and Nature papers. Since 2007, the average, annual publication rate has been around 70 papers in journals with review. In addition to scientific papers, the CBS staff has authored or co-authored many text books and edited proceedings. In 2010, CBS contributed to two cover-story Nature papers: A human gut microbial gene catalogue established by metagenomic sequencing, Nature, 464:132-136, and, Ancient Human Genome Sequence of an Extinct Palaeo-Eskimo, Nature 463:757-762.

CITATION PROFILE
The papers from CBS are widely cited and receive currently more than 5,000 citations per year. The most cited CBS publication has more than 4,000 citations: Identification of prokaryotic and eukaryotic signal peptides and prediction of their cleavage sites, H. Nielsen, J. Engelbrecht, S. Brunak and G. von Heijne, Protein Eng., 10:1-6, 1997, describing a method for prediction of signal peptides in prokaryotic and eukaryotic proteins. Four CBS papers have been included in the ISI Red Hot list for the most cited papers in biology in specific periods, and altogether 10 CBS papers have now more than 500 citations. Except for a single year, CBS has in the 1997-2010 period each year produced a paper, which is among the ten most cited papers out of the approximately 10,000 papers each year co-authored by Danish scientists.

ONLINE SERVICES
CBS has established a highly popular service component. More than 50 servers are available as interactive input forms and access to all the servers is free and unlimited for all academic users, while they are also available on a commercial basis for industrial use. Most of the servers are also available as stand-alone software packages to install and run at the user’s site, with the same functionality. Ready-to-ship packages exist for the most common UNIX platforms. In addition, for many servers, programmatic access is provided in the form of SOAP-based webservices.

TEACHING
CBS has a strong, innovative teaching component with more than 20 highly popular courses in the areas of Bioinformatics, Systems Biology, Human Health, Microbiology and Nutrigenomics – representing important disciplines in the BSc and MSc educations under the Department of Systems Biology. In addition, CBS teaches several highly recognized PhD courses in bioinformatics and systems biology. The teaching strategies at CBS are constantly allowed to evolve in order to facilitate the learning process for all student categories. Since 2005 CBS has offered a variety of courses using real-time internet-transmitted teaching – not only in the form of lectures but also as online teacher-student(s) discussion sessions. Other untraditional teaching actions such as supplementary video modules directed at certain students with a particular need or desire for additional knowledge and in the form of podcasts are also made available from CBS.

EXTERNAL FUNDING
External funding plays an important role in the development and expansion of CBS. A strong focus on external funding does not only allow for growth, it also facilitates collaboration and partnerships with many new partners. External funding accounts for the majority of CBS’ budget; and funding sources include large institutional donors such as the Danish National Research Councils, EU and NIH, as well as numerous private Danish foundations, including but not limited to the Villum Foundation, the Novo Nordisk Foundation and the Lundbeck Foundation.

COMPUTING INFRASTRUCTURE
A strong compute, storage and database infrastructure has been developed since the start of the center in 1993. The compute resources consist of four shared memory servers (SSI Altix, the largest with 8 TB RAM), two Linux clusters (SSI Altix ICE) and a number of dedicated smaller servers.
The data storage exceeds 500 TB, with different types of media ranging from JBODs to close-to-compute fast fiber channel disks. The installation makes use of a 10Gbit/s LAN for efficient communication between the compute and the storage. The center maintains a data warehouse with more than 300 public databases particularly useful in the context of data integration within systems biology. Furthermore, a very large collection of bioinformatics software is installed. The Danish Center for Scientific Computing, the Villum Foundation and the Novo Nordisk Foundation are among the principal funders of the hardware located at CBS.

ACADEMIC ENVIRONMENT

At any given time around 20 different nationalities from all over the world and many different scientific backgrounds are represented at CBS, making CBS a highly multi-disciplinary center with a strong international profile. Together, the CBS group has key competences within the fields of molecular biology, biochemistry, chemical engineering, chemistry, computer science, mathematics, medicine, pharmacology, physics and statistics. CBS is part of one of the largest departments at the Technical University of Denmark, the Department of Systems Biology, which represents the largest concentration of biotechnological research in Denmark. Through numerous collaborative grants CBS also has strong ties to universities, hospitals and industry both nationally and internationally. CBS’ director, Søren Brunak is also affiliated as professor and founding partner of the Novo Nordisk Foundation Center for Protein Research at the University of Copenhagen, as well as the Novo Nordisk Foundation Center for Biosustainability at DTU, which allows for synergy effects between the centers, close collaboration on projects and allowing PhD students to alternate between the different research environments.

MANAGEMENT

CBS is a research center at the Department of Systems Biology, DTU. Since 1993 CBS has been led by Professor Søren Brunak. Professor Ole Lund acts as the deputy director. Monthly meetings between the group leaders, the secretariat and the systems administration support the overall management of CBS. On a day to day basis all practicalities pertaining to administrative support, finance, human resource and project coordination are managed by the secretariat in collaboration with the department staff.